

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 11 AUG 2005

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Applicant's or agent's file reference 431.F		FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/US2004/024922		International filing date (day/month/year) 30.07.2004	Priority date (day/month/year) 30.07.2003	
International Patent Classification (IPC) or national classification and IPC C07F9/6512, C07F9/653, A61K31/675				
Applicant GILEAD SCIENCES, INC. et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input checked="" type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 17.03.2005		Date of completion of this report 09.08.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Klein, D Telephone No. +49 89 2399-		



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/US2004/024922

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-133 as originally filed

Claims, Numbers

1-24 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
 - ☒ claims Nos. 10
because:
 - ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
 - ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 10 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet
 - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - ☐ no international search report has been established for the said claims Nos.
 - ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
 - ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
 - ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☒ all parts.
 - ☐ the parts relating to claims Nos. .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2,5,8-9,15,18
	No: Claims	1,3,4,6,7,11-14,16,17,19-24
Inventive step (IS)	Yes: Claims	2
	No: Claims	1,3-9,11-24
Industrial applicability (IA)	Yes: Claims	1-9,11-18,23-24
	No: Claims	19-22

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item II

Priority :

WO 03/087298 and US 2004/014722D1 which are an intermediate document, are not prior art according to the Chap II PCT proceedings.

Nevertheless, the extensive examination of that document, on the question whether it constitutes prior art or not, will depend essentially on the analysis of the claimed priority rights of the present application and will only be performed in the regional European proceedings to come.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The subject-matter of claim 10 is unclear contrary to Art. 6 PCT, the reason being that claim 10, wherein $R^3=H$, is dependant on claim 3 wherein $R^3= C_1-C_8$ alkyl. Therefore claim 10 will not be examined.

Re Item IV

Lack of unity of invention

This Authority considers that there are 2 inventions covered by the claims indicated as follows:

- I: Claims 1(part)-24(part) consisting in compounds bearing one $-PY^1(Y^2H)_2$ terminal group (Formula of claim 1 or 11 wherein $M2=0$ and $Rx = H$).
- II: Claims 1(part)-24(part) consisting in compounds bearing a terminal group other than one $-PY^1(Y^2H)_2$ (Formula of claim 1 or 11 wherein Rx is different than H).

The common concept linking both invention I and II are antiviral compounds of the formula depicted in claim 11. However this common concept is already known, see for ex D1 (US-A-4 808 716) Formula V or D2 (US 2003/004345) examples 3 and 6.

Hence, this Authority considers that the above-mentioned inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: US-A-4 808 716 (HOLY ANTONIN ET AL) 28 February 1989 (1989-02-28)
- D2: US 2003/004345 A1 (CASARA PATRICK ET AL) 2 January 2003 (2003-01-02)
- D3: EP-A-0 269 947 (BRISTOL MYERS CO) 8 June 1988 (1988-06-08)
- D4: KIM, CHOUNG UN ET AL: "Synthesis and antiviral activity of (S)-9-[4-hydroxy-3- (phosphonomethoxy)butyl]guanine" JOURNAL OF MEDICINAL CHEMISTRY , 33(6), 1797-800 CODEN: JMCMAR; ISSN: 0022-2623, 1990, XP001204580

1) Novelty of Invention I:

D1 discloses compounds of Formula V wherein R1 can be a methyl or hydroxymethyl group and thus anticipate the subject-matter of claims 1,3,4,11,12,13,14,23,24.

D3 discloses compounds of Formulas 3,14,15 and thus anticipate the subject-matter of claims 1,6,7,11,12,16,17,19-24.

D4 discloses on page 56 compound 40 which anticipate the subject-matter of claims 1,11,12,23,24.

Thus claims 1,3,4,6,7,11-14,16,17,19-24 do not comply with the requirements of Art. 33(1) and 33(2) PCT.

2) Inventive step of Invention I:

Claim 2 :

The compounds of claim 2 wherein R^1 - R^8 are each H and wherein M2 is O and Rx is H (by extension Y^1 and Y^2 cannot be both O) are not suggested in the prior art. Therefore, claim 2 complies with the requirements of Art 33(3) PCT.

Claims 5,8,15,18 :

Claims 5/15 and 8/18 respectively differ from D1/D4 by the length of the R^3/R^5 side chains, more precisely a hydroxyethyl instead of a hydromymethyl in D1/D4.

Since it is common practice of organic chemists who are concerned with the preparation of new drugs to take some compound known to possess some interesting pharmacological properties as a model to study the effect of making changes in its structure, the man skilled in the art would, in the present case, slightly modify the functional group fixed on R^3 or R^5 from D1/D4 (elongate the side chain by one methylene group), and would therefore arrive, without the presence of inventive skill to the subject-matter of claims 5,8,15,18.

Claim 10 :

The subject-matter of claim 9 is not considered inventive for the ethylidene group present in the formula is already disclosed in D2. Thus the subject-matter of claim 9 is a mere combination of features known from the prior art.

3) Industrial application :

For the assessment of the present claims 19-22 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.